

**Amendments to the Specification:**

Please replace the paragraph on page 11, lines 14 and 15 with the following rewritten paragraph:

Figure 7 (a-f) depicts autoradiography of [<sup>3</sup>H]ucb 30889 binding to coronal sections of rat brain.

Please replace the paragraph on page 11, lines 16 and 17 with the following rewritten paragraph:

Figure 8 (a-d) depicts the subcellular distribution of [<sup>3</sup>H]ucb 30889 binding within rat brain.

Please replace the paragraph on page 11, lines 20 and 21 with the following rewritten paragraph:

Figure 10 (a and b) depicts the photolabelling of the LBS by [<sup>3</sup>H]ucb 30889 and irreversibility of the complex. Crude synaptosomes (●, closed symbols) were preincubated with [<sup>3</sup>H]ucb 30889 then irradiated with UV light and washed. Nonspecific binding (○, open symbol) was determined using levetiracetam.

Please replace the paragraph on page 11, lines 23 to 25 with the following rewritten paragraph:

Figure 12 (a A and b B) depicts immunostained lysates of the COS-7 cells transfected with SV2A, crude rat brain membranes, and several different PC12 lysates with different levels of LBS.

Please replace the paragraph on page 11, line 31 with the following rewritten paragraph:

Figure 15 (a and b) depicts the structure of (A) levetiracetam and (B) ucb 30889.

Please replace the paragraph on page 12, lines 1-8 with the following rewritten paragraph:

Figure 16 (a A and b B) depicts binding of [<sup>3</sup>H]ucb 30889 to brain membranes. A. Binding of [<sup>3</sup>H]ucb 30889 to brain membranes from SV2A, SV2B, and SV2A/SV2B

knockout mice. [ $^3\text{H}$ ]ucb 30889 alone (□) [ $^3\text{H}$ ]ucb 30889 plus 1mM LEV (■). Error bars are the SD of experiments performed with 5 wildtype brains and 4 KO brains. Each experiment was performed in triplicate. B. Western blot of brain membranes from wild type and homozygous knockout mice probed with an anti-SV2 monoclonal antibody (cross-reactive to all isoforms, SV2A, SV2B and SV2C). LANES 1: wt; 2: SV2A ko; 3 SV2B ko; 4: SV2A/B double ko.

Please replace the paragraph on page 12, lines 9 to 15 with the following rewritten paragraph:

Figure 17 (a A and b B) depicts binding of [ $^3\text{H}$ ]ucb 30889 to COS-7 cells expressing hSV2A. A. Binding of [ $^3\text{H}$ ]ucb 30889 to hSV2A transiently expressed in COS-7 cells. [ $^3\text{H}$ ]ucb 30889 is tested for binding to either untransfected COS-7 cells, or COS-7 cells transiently expressing either  $\beta$ -gal or hSV2A. [ $^3\text{H}$ ]ucb 30889 alone (□) [ $^3\text{H}$ ]ucb 30889 plus 1mM LEV (■). B. IC<sub>50</sub> curves of LEV, ucb L060, ucb 30889 against hSV2A transiently expressed in COS-7, in the presence of [ $^3\text{H}$ ]ucb 30889. LEV ( $\Delta$ ) ucb 30889 (■) ucb L060 (●). Error bars are SEM, n=3.

Please replace the paragraph on page 12, lines 16 to 22 with the following rewritten paragraph:

Figure 18 (a A and b B) depicts binding of [ $^3\text{H}$ ]ucb 30889 in the presence of competing drugs. A. Correlation of binding of a series of LEV compounds to mouse brain and to hSV2A, pIC<sub>50</sub>s measured against [ $^3\text{H}$ ]ucb 30889. The pIC<sub>50</sub> values are the mean of two independent experiments, where each determination lies within 0.2 log units of the mean. B. Correlation of binding of a series of LEV family compounds to hSV2A assayed in transiently transfected COS-7 cells, pIC<sub>50</sub>s measured against [ $^3\text{H}$ ]ucb 30889, and of anti-seizure potencies in the mouse audiogenic model.

Please replace the paragraph on page 12, lines 27 to 31 with the following rewritten paragraph:

Figure 21 (a, b, and c ~~A, B, and C~~) depicts preparation of soluble SV2A and quantitation of by binding assay. A. Detection by western blot using anti-SV2A antibodies of soluble SV2A in the supernatant of solubilized rat brain membranes. B. Analysis of the ability of

levetiracetam and ucb 30889 to specifically bind to soluble SV2A. C. Scatchard analysis indicates that the  $K_D$  for the binding of [ $^3H$ ] ucb 30889 to SV2A in native rat brain membrane is 30 nM, while that for the soluble protein is 82 nM.

Please replace the paragraph on page 13, lines 2 to 4 with the following rewritten paragraph:

Figure 22 (a and b) depicts identification of SV2A partners. Western blot analysis show synaptotagmin associated to soluble SV2A in the immunopurified fractions of the supernatants from solubilized rat brain membranes. The isoform SV2B was not detected.